Treatment Scoring of Unruptured Intracranial Aneurysms

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Abstract

Background and Purpose My purpose was to obtain a reliable treatment score for unruptured intracranial aneurysms (UIAs) from variables known at baseline.

Methods The series included 142 patients with UIAs diagnosed between 1956 and 1978, when UIAs were not treated and were followed up until the first aneurysm rupture, death or the last contact. Previously published unruptured intracranial aneurysm treatment scores (UIATS) were recorded and finally was a new treatment score was constructed.

Results The median follow-up time was 21.0 years (IQR10.4-31.8 years). A total of 34 patients had an aneurysm rupture during 3064 person-years of follow-up. The UIATS differed slightly between those with and without an aneurysm rupture (9.4$\pm$2.8 vs. 8.3$\pm$3.1,p=0.082). The receiver operating characteristics curve of the UIATS for predicting rupture showed a modest area under the curve (AUC) (0.602, 95% CI 0.495-0.709, p=0.074). The best new treatment score consisted of 4 variables: age <40 years (2 points), current smoking (2 points), UIA size $\geq$7 mm (3 points) and location (anterior communicating artery, 5 points; internal carotid bifurcation, 4 points, and posterior communicating artery, 2 points). Scores of 5–12 points were associated with high cumulative UIA rupture rates (16%–60% at 10 years and 49%–80% at 30 years), favoring UIA treatment. Scores of 1–4 points (3% at 10 years and 18% at 30 years) favored conservative treatment and needed additional indications for treatment. Patients with a score of 0 points should not be treated (no ruptures during 513 follow-up years). The AUC for this scoring was 0.755 (95%CI 0.657–0.853, p<0.001) and was better than that of the UIATS (p=0.02).

Conclusions This new simple and rapid scoring system is quite reliable for evaluating treatment indications with regard to the lifelong prevention of aneurysm rupture.

INTRODUCTION

Subarachnoid hemorrhage (SAH) is a serious disease,[1-4] but its incidence is gradually decreasing[5,6] and the mean age of patients is increasing.[2,6] The decrease in incidence predominantly in the younger age groups is probably due to a reduction in cigarette smoking in the general population, and perhaps also to more precise SAH diagnoses.[5,6]

To prevent SAH occlusion of unruptured intracranial aneurysms (UIAs) has been performed for the last 40 years.[4,7,8] At the same time, the increasing use of MRI for examining symptoms unrelated to UIAs (chronic headache, dizziness, vascular diseases, dementia, etc.) has led to the detection of more asymptomatic UIAs than previously.[4,7,8] Since the prevalence of aneurysms is not decreasing,[9] probably their lower rupture risk has resulted in lower SAH incidence rates. The decrease in SAH incidence combined with the increase in the discovery of UIAs has made interpretation of the indications for treating UIAs more difficult.

The indications for UIA treatment were in any case already challenging because of a lack of factually based prospective natural history studies. This was due to differences in the selection of UIA patients for conservative follow-up, majority of whom were considered to have a low risk of rupture, while some had a shorter life expectancy or higher treatment risks.[10] True new natural history studies of UIAs are impossible nowadays without treatment selection bias. An unruptured intracranial aneurysm treatment score (UIATS) based on the opinions of 69 worldwide experts has been published recently,[8] but unfortunately it was relatively complex, did not include patient data and lacked validation.

There is, however, one almost lifelong prospective follow-up study of UIAs among patients of working age[1,11-13] which was not subject to treatment selection bias and was considered to be of the highest quality and to have the least sources of bias of all known UIA studies.[10,14] This also investigated the validity of its UIATS and searched for a new treatment score from variables known at baseline which could better predict the lifelong rupture rate.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patients

This study included 142 European white patients (median age 42, range 15–61 years; 76 women) with 182 UIAs diagnosed at the Department of Neurosurgery, Helsinki University Central Hospital, between 1956 and 1978, when UIAs were not operated on in Finland. This hospital was responsible for neurosurgical services for almost the whole Finnish population at that time.[12,15] For details of the cohort and the examinations performed, see the previous follow-up reports.[1,10-13,15] Approval for the surveys and the collecting of follow-up data had been obtained from the local ethics committee in compliance with national legislation and the Declaration of Helsinki.

Of the 142 patients with UIAs, 131 had a prior SAH with multiple aneurysms at baseline. Only the verified ruptured aneurysm was operated on, and occlusion of the aneurysm without sacrifice of the parent vessel was confirmed by postoperative angiography.

Follow-up methods

Detailed follow-up protocols have been reported previously.[1,10-13,15-19] Briefly, the follow-up of the patients was based on outpatient clinic visits, postal questionnaires and telephone interviews obtained from patients and/or proxies every 10 years from the early 1960's onwards. The structured questionnaire included patient characteristics, previous diseases, hospital visits, medication and health behavior. The last patient follow-up was performed in 2012, when 20 patients were alive without rupture of the UIA.[12,13,15,19] By the end of follow-up 113 (80%) had died and of them 86 of causes unrelated to UIAs.[15]

Additional information on all the patients was obtained from medical records supplied by other hospitals and general practitioners, and the accuracy of the data with regard to diseases, medication, health behavior and blood pressure (BP) levels was verified. Autopsy reports and official death certificates were examined for all deceased patients. In Finland a statutory medico-legal autopsy is performed on all those who die due to trauma or unknown causes (Act on the Inquest into the Cause of Death, 459/1973, Finnish Law). The follow-up was complete.

Risk factors

The UIATS[7,8] variables for each patient were recorded using only those known at the baseline (Table 1). Hypertension was defined as a systolic pressure repeatedly greater than 140 mm Hg, a diastolic pressure greater than 90 mm Hg, or use of antihypertensive medication.[15,16] Current smoking was ascertained at baseline, and alcohol consumption was recorded in approximate grams of absolute ethanol consumed within one week (1 standard drink = 12 g of alcohol). A family history of SAH was defined as ≥2 first-degree relatives with verified ruptured aneurysms.

Aneurysm measurements

All angiographies performed at baseline were examined by a neuroradiologist who had no knowledge of the patients' case histories.[11,13,17] The maximum diameter (D) of the UIAs, together with their neck width (n), was measured from standard projections of 2D conventional angiograms at baseline and used to calculate the aspect ratio (D/n).[13,19] The size ratio was not available. Also recorded were the location and shape of the UIA (round, oval, irregular or lobulate). Aneurysm growth rates and de novo aneurysm formation, which have been reported previously, were not used here since the time between diagnosis and the control angiogram (median 22 years) was too long to be used as a predictive variable.[11,13,17,19]

Statistical analysis

The data were analyzed with IBM SPSS Statistics, version 24.0, for Windows (IBM Corp., Armonk, NY, USA). UIATS variables at baseline were compared by reference to future aneurysm rupture status using Fisher's exact test or the Pearson Chi-square test. Sum scores [expressed as mean ± standard deviation (SD) and median with interquartile range (IQR)] were compared with t-tests and the Mann-Whitney U- test. Sensitivity, specificity and positive and negative predictive values were calculated for the UIATS.

Cox proportional hazards regression with a forward stepwise procedure (entry into the model if $p < 0.15$) and Wald statistics was employed to estimate hazard ratios (HRs) and 95% confidence intervals

(CIs) to test the predictors of future aneurysm rupture. Each patient was followed up until SAH, death from a cause other than SAH, treatment of the UIA (3 cases with a follow-up lasting >24.4 years), or the last follow-up contact. The test of significance was based on changes in the log (partial) likelihood. The variables known at the beginning of the follow-up were sex, location of the largest UIA, and the UIATS variables. The proportionality assumption was confirmed. The grouping of the variables was the same as that of the UIATS.

The new integer risk score points were based on the regression coefficients in the final Cox proportional hazards model, the areas under the curve (AUC) for the receiver operating curves (ROC) being calculated for both the UIATS and the new prognostic treatment scores. The C-statistic with 95% CIs was used to test how the total scores matched the observed rupture rates, the AUC between scores being analyzed using the technique of Hanley and McNeil.[20] This statistical analysis was performed using MedCalc for Windows, version 18.9 (MedCalc Software, Ostend, Belgium). The cumulative probabilities of aneurysm rupture at 10 and 30 years after the diagnosis according to the new score groups was calculated by performing the Kaplan–Meier product-limit analysis. A two-tailed P value <0.05 was considered statistically significant.

RESULTS

Patient characteristics and follow-up

During a total follow-up of the 142 patients (median 21.0 years, range 0.8–52.3 years per patient) for 3064 person-years 34 patients (24%) had an aneurysm rupture from an UIA (approximate annual incidence, 1.1%). The cumulative rate of SAH was 11% (95% CI, 5–16%) at 10 years and 30% (21–39%) at 30 years. The median follow-up time between diagnosis and a subsequent aneurysm rupture was 10.6 years (range 1.2–24.2 years), and that of patients without a rupture 24.4 years (range 0.8–52.3 years).

UIATS of patients

The UIATS factors of the patients, stratified by their later aneurysm rupture status, are shown in Table 1. UIATS was only slightly higher in those with a rupture than in those without (p=0.087). The UIATS favored UIA repair in 141 patients, giving a high sensitivity of UIATS in detecting cases with aneurysm rupture (100%) but very low specificity (1%). All patients were Finns and most had a prior SAH. If these were not taken into account UIATS was slightly higher in those with a later rupture (3.44±2.84 vs. 2.34±3.11, p=0.069). UIATS predicted UIA rupture relatively modestly: sensitivity 20/34 (59%), specificity 58/108 (54%), positive predictive value 20/70 (28%), and negative predictive value 58/72 (81%).

Current smoking was missing from the data for 6 of the 34 patients with an aneurysm rupture (18%) and 13 of the 108 without a rupture (12%). The mean score per patient was 8.55+3.04 if patients without smoking information were excluded and the mean scores by later rupture status were 9.43±2.77(range 3–13) vs. 8.29±3.08 (3–15) (p=0.082).

Risk factors for UIA rupture and the new treatment score

All the UIATS factors with additional UIA locations and sex were tested with Cox regression analysis to identify the variables which best predicted a future aneurysm rupture. Age <40 years, aneurysm diameter ≥7 mm, current smoking, UIA located either in the internal carotid bifurcation or in the anterior (ACOA) or posterior communicating arteries (PCOA) predicted a subsequent rupture (Table 2). Although women had aneurysm ruptures more frequently than men (23 of the 76 women vs. 11 of the 66 men), female sex was not an independent risk factor for aneurysm rupture (HR 1.54, 95% CI 0.64-3.71, p=0.34). A new system for scoring UIA treatment was constructed from the regression coefficients of the 4 variables (Table 2).

The AUC for the ROC of simple scoring (points 0 vs. 1 for 4 variables; sum score 1, Figure 1) was fair (AUC 0.730, SE 0.052, 95%CI 0.628-0.831, p<0.001), and that for the wider scoring curve (score sum range 0-12;sum score 2 in Figure 1) was somewhat better (0.755, SE 0.050, 95%CI 0.657-0.853, p<0.001), but that for the UIATS was no more than modest (0.618, SE 0.059, 95% CI 0.502-0.733, p=0.059). The inclusion of sex in the scoring (women vs. men, 2 vs. 0 points) did not improve the ROC

curve (sum score 3 range 0-14; 0.766, SE 0.049, 95%CI 0.669-0.863, p<0.001; Figure 1). The new scores did not differ significantly from one another but all these were better than UIATS (p<0.05). The optimal cut-off point was obtained with the sum score 2 at ≥5 vs. <5 points for sensitivity (0.607) and specificity (0.789) (Figure 1 and Table 3).

The new scores differed with respect to future aneurysm rupture status. The sum score 1 with the use of 0 vs. 1 for each of the 4 predictors was higher (p<0.001) in those with a later rupture than in those without (2.18±0.86 vs. 1.35+0.92), as was the difference between the scores with the wider scoring (sum score 2, 5.32±2.36 vs. 3.04±2.23, p<0.001).

Sum score 2 was grouped into 4 categories according to the long-term cumulative aneurysm rupture rates and predicted future aneurysm rupture (p<0.001) (Table 3, Figure 2). 18 patients with a treatment score of 0 seem not to need UIA occlusion treatment (annual incidence 0%, 95% CI 0-0.72%). 14 of these patients were non-smokers aged ≥40 years and had small (<7 mm) middle cerebral artery aneurysms. None of them had a rupture during 385 follow-up years (approximate annual incidence 0%, 95% CI 0-0.96%).

On the other hand, patients with scores in the range 5-12 should be treated, since their aneurysms have a high cumulative UIA rupture risk. Patients with scores 1-4 should be individually evaluated, taking into account other rupture and treatment-associated factors (experience and the results of treatment), life expectancy and also whether cessation of smoking can reduce the risk still further.

If smoking is excluded from sum score 2 because of missing values in 19 cases, AUC decreased (0.708, SE 0.054, 95%CI 0.603-0.814, p<0.001) and the optimal cut-off point was at ≥4 vs. <4 points for sensitivity (0.529) and specificity (0.824).

DISCUSSION

The treatment score obtained from this prospective study with an almost lifelong follow-up and a very low treatment selection bias suggests that treatment of UIAs among patients of working age can be estimated quite reliably with only 4 variables at baseline. Patient age (< 40 years), cigarette smoking, aneurysm size (diameter ≥ 7 mm), and location in the ACOA, PCOA or internal carotid bifurcation

determine the risk of UIA rupture significantly better than does the UIATS. The small middle cerebral artery aneurysms (<7 mm) in non-smokers aged ≥40 years seem to have so low a rupture risk that they can be treated conservatively.

Simultaneously with the discovery of increasing numbers of UIAs, it is likely that the indications for treatment will decrease, because of the decline in the prevalence of smoking and the incidence of SAH,[6] and because of the discovery of incidental UIAs in older people than previously. These patients are also less likely to be smokers or to have higher treatment risks because of age.[21] Existing aneurysms are also less likely to rupture in the future if smoking decreases further.[12,19] The cost-effectiveness ratio of UIA treatment is thus increasing. Treatment scores have not previously been calculated from patient-based data to prevent life-time aneurysm rupture risk.

Since the results of the various studies of risk factors affecting UIA rupture and growth differ an attempt was made to improve the reliability of treatment recommendations by means of a UIATS.[7,8] The study concerned did not include patient data, however, but was based on the opinions of 69 worldwide aneurysm treatment experts. The UIATS included several variables but was lacking in any validation. The present study shows that UIATS overestimates the treatment indications of patients of working age and that its specificity for the lifelong occurrence of UIA rupture is low and its predictive value in terms of ROC was modest. Most of the present patients obtained 6 UIATS points, only because of their prior SAH history and Finnish nationality. The UIATS recommended UIA treatment for 99% of the patients, but 24% had an aneurysm rupture. The UIATS score specificity seemed to be markedly reduced by these two variables.

The UIATS reflects treatment policy in recent decades, during which time the proportion of treated UIAs increased[10,21,22] simultaneously with the discovery of UIAs and the introduction of endovascular treatment for older patients as well and for those with increased treatment risks. The cost-effectiveness ratio will probably also have increased over that period since more and more UIAs which would never have ruptured were being treated, but the mortality rates associated with the treatment, 1-2%, and the morbidity of approximately 10% remained constant.[21] The overestimation of UIA treatment associated with the UIATS may also have been due to patients' fears of a possible aneurysm rupture and in part also

to conflicts of interest, enthusiasm, or perhaps economic considerations, since the consultants involved were treating UIAs as part of their gainful employment. A similar overtreatment in real-world practice with a low AUC value was seen when UIATS was coded for patients with UIA treatment.[23] Thus there was a clear need a treatment scoring system based on patient data with reliably measurable variables at baseline.

The present results show that even though small UIAs in patients of working age can rupture during the remaining life time, the majority of these do not. These patients are usually healthy, without any chronic diseases and without any evident contraindications for treatment. Life expectancy is shortened of principally among patients with UIAs who are aged < 40 years at baseline and who have a later aneurysm rupture.[15,19] Such patients usually show clear indications for treatment irrespective of the size of the aneurysm, particularly if they smoke, since the cumulative rupture risks at 10 and 30 years are quite high. Long-term smoking increases the risk for UIA growth, which in turn can result in rupture.[19] In addition, if the UIA is located in the ACOA, PCOA or internal carotid bifurcation the indication for treatment will be even higher.[10,12,21,22] Although ACOA and PCOA aneurysms are known to carry a higher rupture risk than other aneurysms, the risk may be even higher than has previously been shown because these UIAs have more frequently been treated at baseline than have posterior circulation UIAs, for example.[10,21,22] Posterior circulation UIAs may also have higher rupture risk, which may possibly have been obscured in the present series because of the small number of such cases. On the other hand, a significantly higher rupture risk was seen here in internal carotid bifurcation UIAs, an aneurysm location that is known to be more frequent in young adults and is associated with a higher growth rate.[19]

The present treatment score predicted long-term UIA ruptures better than did any of the separate factors alone, so that those with a score of at least 5 points had a mean cumulative rupture risk of 50% at 30 years. This favors treatment if the risk cannot be reduced, e.g. by cessation of smoking. Indeed, the latter may even be a treatment option if the score can be reduced to a level which favors conservative treatment.[24-27] Women are known to have a higher incidence of SAH than men, partly because they have a longer life expectancy and a higher prevalence of aneurysms (approximately 1.6-fold).[9,28] It is also known that, despite their lower prevalence of smoking, women also have a higher aneurysm growth rate

than men,[11,14,19] but even so, the addition of female sex to the predictive factors did not improve the score in the present study.

The strengths of this study lie in the complete and almost lifelong follow-up and the very limited treatment selection bias.[12,27] Correspondingly, this cohort was considered previously to be of high quality for research purposes and to have low sources of bias relative to those used in other UIA studies.[10,14] Finnish people have been considered to be subject to a higher risk of aneurysm rupture,[10] but the Finnish cohort has proved to be the only one in the PHASES score study that represented a true natural history of the condition. The incidence of SAH is no higher in Finland than elsewhere when standardized for the study design with its inclusion and exclusion criteria, the accuracy of diagnosis and the sex and age distributions of the population.[6] The Nordic countries seem to have similar incidences of SAH.

One limitation of the study is the relatively small sample size despite a long total follow-up time as compared with prospective multicenter study populations, which have on the other hand had shorter follow-ups and high treatment selection bias. Patients with a prior history of SAH have not been shown to have a significantly higher risk of aneurysm rupture than others when confounding factors are taken into account.[10] Additional controlling for smoking would have reduced the possible association between prior SAH and the risk of UIA rupture, since smoking affects both aneurysm rupturing and the occurrence of multiple aneurysms. Only one smaller prospective Japanese study has suggested that prior SAH might increase the risk of SAH, but in that instance smoking was not taken into account.[10] Our patients were also younger than those in the other studies. Patients of working age are usually treated nowadays, which has led to biased results with regard to the natural history of UIAs. Elderly patients with small UIAs are more likely to be left untreated, because of the low UIA rupture rate. Also, these results should not be used explicitly for recommending the treatment of small (<7 mm) ACOA aneurysms in non-smoking 70-80-year-old female patients, even when the score sum is 5.

In conclusion, this new simple and rapid scoring system is better than UIATS for evaluating treatment indications and achieving lifelong prevention of UIA ruptures. The findings suggest that UIAs in patients of working age can be treated with a better focus and improved cost-effectiveness provided

that this is undertaken by experienced physicians achieving good treatment results. This scoring system still requires validation in a new cohort of patients.

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Disclosures

None.

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Figure 1. Receiver operating characteristic (ROC) curves for predicting the long-term rupture risk of unruptured intracranial aneurysms.

All the new scores predicted long-term aneurysm rupture better ($p<0.05$) than the previously used unruptured intracranial aneurysm treatment score (UIATS). See text for detailed calculations of the areas under the receiver operating characteristic curves.

Figure 2. Long-term cumulative aneurysm rupture risk of treatment score (sum score 2).

A score $\geq$ 5 points favors aneurysm treatment, while aneurysms with scores of 0 points are better treated conservatively. Cumulative aneurysm rupture figures differed significantly between the groups ($p<0.001$).

Table1. Unruptured intracranial aneurysm treatment scores (UIATS) stratified by aneurysm rupture status

Factor	Category/ Score points	Patients with SAH (n=34, 24%)	Patients without SAH (n=108, 76%)	All patients (n=142, 100%)
Age (single)(%)*	< 40 years / 4	20 (34)	38 (66)	58 (100)
	40-60 years / 3	14 (17)	70 (83)	84 (100)
	61-70 years / 2	0	0	0
	71-80 years / 1	0	0	0
	>80 years / 0	0	0	0
Risk factor incidence (multiple)(%)	Previous SAH from a different aneurysm /4	31 (24)	100 (76)	131 (100)
	Familial intracranial aneurysms or SAH / 3	3 (33)	6 (67)	9 (100)
	Finnish ethnicity / 2	34 (24)	108 (76)	142 (100)
	Current cigarette smoking / 3	20 (29)	50 (71)	70 (100)
	Hypertension / 2	13(27)	36 (73)	49 (100)
	Autosomal-polycystic kidney disease / 2	1 (50)	1 (50)	2 (100)
	Current drug abuse / 2	0	0	0
	Current alcohol abuse /1	5 (24)	16 (76)	21 (100)
Clinical symptoms related to UIA (multiple)(%)	Cranial nerve deficit /4	3 (60)	2 (40)	5 (100)
	Clinical or radiological mass effect /4	1 (25)	3 (75)	4 (100)
	Thromboembolic event from the aneurysm /3	0	1 (100)	1 (100)
	Epilepsy	0	0	0
Other (multiple)(%)	Reduced quality of life due to fear of rupture /2	0	0	0
	Aneurysm multiplicity /1	7 (21)	26 (79)	33 (100)
Maximum diameter (single)(%)	<4.0 mm / 0	15 (29)	36 (71)	51 (100)
	4.0-6.9 mm / 1	9 (14)	56 (86)	65 (100)
	7.0-12.9 mm / 2	8 (38)	13 (62)	21 (100)
	13.0-24.9 mm / 3	1 (33)	2 (67)	3 (100)

	>24.9 mm / 4	1 (50)	1 (50)	2 (100)
Morphology (multiple)(%)	Irregularity or lobulation / 3	3 (14)	19 (86)	22 (100)
	Aspect ratio >1.6 or size ratio >3 / 1	14 (22)	51 (78)	65 (100)
Location (single)(%)	BasA bifurcation / 5	0	2 (100)	2 (100)
	Vertebral/basilar artery / 4	0	2 (100)	2 (100)
	AcomA/pcomA / 2	14 (34)	27 (66)	41 (100)
	MCA / 0	15 (23)	49 (77)	64 (100)
Life expectancy due to chronic and/or malignant diseases (single)(%)	<5 years / -4	0	2 (100)	2 (100)
	5-10years / -3	0	4 (100)	4 (100)
	>10 years / -1	0	7 (100)	7 (100)
Co-morbid disease (multiple)(%)	Neurocognitive disorder / -3	0	1 (100)	1 (100)
	Psychiatric disease or coagulopathy / -2	0	3 (100)	3 (100)
Age-related risk (single)(%)*	< 40 years / 0	20 (34)	38 (66)	58 (100)
	40-60 years / -1	14 (17)	70 (83)	84 (100)
Aneurysm size-related risk (single)(%)	<6.0 mm / 0	22 (21)	85 (79)	107 (100)
	6.0-10.0 mm / -1	9 (32)	19 (68)	28 (100)
	10.1-20.0 mm / -3	2 (40)	3 (60)	5 (100)
	>20 mm / -5	1 (50)	1 (50)	2 (100)
Aneurysm complexity-related risk (single)(%)	High / -3	3 (50)	3 (50)	6 (100)
	Low/ 0	31 (23)	105 (77)	136 (100)
Intervention-related risk	Constant / -5	34	108	142
UIATS	Mean (SD)	9.09(2.83)	8.05(3.14)	8.30(3.09)
	Median (IQR)	9 (7-12)	8 (5-10)	8 (6-11)
	Total score sum/no. patients	309/34	869/108	1178/142
UIATS score recommendation	Favors UIA repair (%)	34 (24)	107 (76)	141 (100)
	“not definitive”(%)	0	1 (100)	1 (100)
UIATS score recommendation without Finnish ethnicity	Favors UIA repair (%)	33 (26)	95 (74)	128 (100)
	“not definitive”(%)	1 (8)	12 (92)	13 (100)
	Favors conservative management (%)	0	1 (100)	1 (100)

UIA = unruptured intracranial aneurysm; SAH = subarachnoid hemorrhage; AcomA = anterior communicating artery; A2 = pericallosal artery; BasA = basilar artery; MCA= middle cerebral artery; IQR = interquartile range (range between 25th and 75th percentiles); pcomA = posterior communicating artery; SAH = subarachoid hemorrhage; UIATS score = unruptured intracranial aneurysm treatment score.

UIATS vs. SAH in all the patients: sensitivity = 100%, specificity = 1%, positive predictive value = 24%, negative predictive value = 100%.

UIATS vs. SAH in all patients without Finnish ethnicity: sensitivity = 97%, specificity = 12%, positive predictive value = 26%, negative predictive value = 93%.

*p<0.05

Table2. Univariable and multivariable Cox regression analyses of risk factors for aneurysm rupture

	Univariable			Multivariable			Aneurysm rupture risk score points*
	Regression coefficient	Standard error	Hazard ratio (95% CI)	Regression coefficient	Standard error	Hazard ratio (95% CI)	
Age at diagnosis <40 years)	0.649	0.349	1.91 (0.97-3.79)	0.778	0.442	2.18 (0.92-5.18)	2
Current smoking at baseline	0.913	0.420	2.49 (1.10-5.67)†	0.682	0.454	1.98 (0.81-4.81)	2
Maximum diameter of unruptured aneurysm (≥7 mm)	0.811	0.378	2.25 (1.07-4.72)†	1.125	0.422	3.08 (1.35-7.04)‡	3
Aneurysm location							
Anterior communicating artery	0.928	0.533	2.53 (0.89-7.18)	1.622	0.589	5.06 (1.59-16.07)‡	5
Internal carotid bifurcation	0.964	0.608	2.62 (0.80-8.63)	1.433	0.660	4.19 (1.15-15.28)†	4
Posterior communicating artery	0.429	0.377	1.54 (0.73-3.21)	0.741	0.476	2.10 (0.83-5.33)	2

Of the 33 patients with posterior communicating artery aneurysms, 10 (30%) suffered a rupture, as did 4 of 8 (50%) anterior communicating and 3 of 8 (38%) internal bifurcation carotid artery aneurysms.

*Total risk sum score range 0 to 12. Scores of other categories of variables, 0 points

†p<0.05
‡p<0.01

Table 3. Risk sum score and cumulative incidence of aneurysm rupture

Aneurysm rupture risk score points*	No. of patients (%)	Annual rupture rate (%)	Cumulative rupture rates, % (95% CI)	
			10 years	30 years
0	18	0 (0/513)	0	0
1-4	68	0.6 (11/1722)	3 (0-8)	18 (8-28)
5-8	32	2.2 (13/594)	16 (3-29)	49 (29-70)
9-12	5	6.8 (4/59)	60 (17-100)	80 (44-100)
Total	123	1.0 (28/2888)	11 (5-16)	30 (21-39)

The annual rupture rate is calculated by dividing number of patients with an aneurysm rupture by the person-years of follow-up, shown in parentheses. CI indicates confidence intervals.

Use of 5-12 points as a recommendation for aneurysm treatment gives a sensitivity 61%, specificity 79%, positive predictive value 46% and negative predictive value 87%.

*$p<0.001$, log-rank test for differences in cumulative rupture rates between score groups